

U.S. Patent Application No.: 09/964,240  
AMENDMENT A

ATTORNEY DOCKET NO.: 3974.002

**REMARKS**

Claims 3-12 are pending. Claims 3, 4, and 6-10, are amended herein. New claims 17-19 are added to better claim that which the Applicant regards as his invention. Support for new claims 17-19 may be found, for example, at ¶[0050] and in Example 10 of the specification. Applicant asserts that no new matter has been introduced, and entry of the amended and new claims are respectfully requested.

**Rejection of Claims under 35 U.S.C. §112, ¶2**

Claims 4, 6, and 7-12 stand rejected as being allegedly indefinite.

With respect to claims 4 and 8, the allegedly indefinite phrase "wherein the vaccine or medicament comprises a nucleic acid vaccine or medicament" has been deleted and the claims further amended to clarify, in the form of a Markush group, the vaccine encompassed by these claims. Support for this amendment may be found, for example, at ¶¶[0006]-[0008] of the specification. Applicant believes that claims 4 and 8 as amended herein are not indefinite, and respectfully requests that this rejection be withdrawn.

With respect to claim 6, the Examiner's suggestions to depend claim 6 from 3 and to recite the steps of claim 6 in alphabetical order from (a) are gratefully acknowledged, and claim 6 is amended herein in accord with his suggestions. Applicant believes that claim 6 as amended herein is not

indefinite, and respectfully requests that this rejection be withdrawn.

With respect to claim 7, the temporal relationship of steps (a) and (b) is clarified by the amendment to claim 7 herein to include administration of the extract before, during, simultaneously with, or after, the administration of the vaccine. Support for this amendment may be found, for example, at ¶[0050] of the specification. Applicant believes that claim 7 as amended herein is not indefinite, and respectfully requests that this rejection be withdrawn.

With respect to claim 9, the claim is amended herein in accord with the Examiner's suggestion to recite steps (a)-(b). Applicant therefore believes that claim 9 as amended herein is not indefinite, and respectfully requests that this rejection be withdrawn.

With respect to claim 10, this claim is amended to depend from claim 5, rather than from non-elected claim 2. Accordingly, Applicant requests withdrawal of this rejection.

**Rejection of Claims under under 35 U.S.C. §102(a)**

Claims 3, 7, 11, and 12 stand rejected as being allegedly anticipated by Xin (CN 1279107 - DWPI Abstract). Applicant respectfully traverses the rejection on two grounds: (a) that Xin is not prior art, and (b) that the rejection is rendered moot by the amendments to the rejected claims herein.

(a) Applicant submits herewith a Declaration under 37 C.F.R. §1.131 asserting that the date of conception of the rejected claims was prior to the effective date of Xin as a reference. Applicant asserts that conception of the rejected claims occurred prior to June 1, 1999, which is prior to publication date of Xin of January 10, 2001. Applicant provides a showing of facts in the form of a proposal submitted to a potential grantor on June 1, 1999, which discloses the invention of the rejected claims. In addition, Applicant submits with his Declaration evidence of financial support for investigation of the immunological properties of pine-cone extract, showing due diligence in reduction to practice from at least prior to the effective date of Xin to the date of filing of the instant application on September 26, 2001.

Applicants therefore declare that they invented the subject matter of the rejected claims, which includes independent Claims 3 and 7, prior to the effective date of Xin as a reference, and therefore that Xin may not be applied as prior art against their application. Accordingly, Applicant respectfully requests withdrawal the rejection of claims 3, 7, 11, and 12 under 35 U.S.C. §102(a).

(b) Further, Applicant asserts that the rejection is rendered moot by the amendments to the rejected claims herein. Claims 3 and 7 are amended to recite a vaccine rather than a vaccine or medicament. Claim 11 and 12 depend from Claim 7.

Xin does not teach or suggest a vaccine. Therefore, Applicant asserts that Xin cannot anticipate the rejected claims as amended herein, or any of the claims, because Xin does not teach or suggest all of the elements of the claims. Applicant therefore respectfully requests that the rejection be withdrawn.

**Rejection of Claims under under 35 U.S.C. §103(a)**

Claims 3, 4, 7, 8, and 10-12 stand rejected as being allegedly obvious over Xin or Sakagami et al. (U.S. 4,985,249), in view of Sham et al. (U.S. 5,914,332). Applicants respectfully traverse with respect to both combinations of references.

With respect to the rejection over Xin in view of Sham, Applicant notes that the Examiner relies upon Xin for at least the teaching of a pine cone extract (Office Action at page 6, ¶2). Applicant respectfully repeats his argument made above with respect to the rejection for anticipation, that the rejected claims, which includes those additional claims rejected for obviousness (Claims 4, 8 and 10), were conceived prior to the effective date of Xin as a reference, and that therefore Xin is not prior art. Because Sham does not teach all of the elements of the rejected claims, Applicant asserts that, upon the withdrawal of Xin as prior art, a prima facie case of obviousness cannot be established. MPEP 2143. Therefore, Applicant respectfully requests that this rejection be withdrawn.

With respect to the rejection over Sakagami in view of Sham, Applicant respectfully traverses on three grounds.

First, Applicant asserts that neither Sham nor Sakagami teaches an adjuvant within the meaning of the term as used in the rejected claims. The term "adjuvant" has at least two accepted meanings. In general usage, "adjuvant" merely means "serving to help or assist; auxiliary," while in the medical and immunological fields the term means "a substance admixed with an immunogen in order to elicit a more marked immune response." Webster's College Dictionary, 2<sup>nd</sup> edn., 1997. Dorland's Illustrated Medical Dictionary, 25<sup>th</sup> edn., concurs with this dual definition of "adjuvant" as "a substance which aids another; in immunology, any such substance that when mixed with an antigen, enhances antigenicity and gives a superior immune response."

Applicants assert that the term "adjuvant" is used in the present application exclusively in its immunological sense. Thus, for example, adjuvants are defined in the present application at ¶[0009] as "substances, when administered simultaneously with a specific antigen, [that] will enhance the immune response to that antigen."

In contrast, Sham uses the term "adjuvant" exclusively in its general sense. Thus, at col.72, line 2, Sham simply states that "compounds of the present invention may be administered orally, parenterally, sublingually, by inhalation spray,

rectally, or topically in dosage unit formulations containing conventional nontoxic pharmaceutically acceptable carriers, adjuvants, and vehicles as desired" (emphasis added). Sham subsequently defines adjuvants as "...wetting agents, emulsifying and suspending agents" (col 73, line 42).

Sham therefore teaches adjuvants only within the context of a laundry list of auxiliary or helpful compounds to be administered with a retroviral protease inhibitor, and nowhere does Sham teach or suggest an adjuvant in its immunological sense. Sakagami does not remedy this deficiency.

The essence of the present invention is the finding that pine cone extract significantly enhances antigenicity of a vaccine resulting in a superior immune response to vaccination. The pine cone adjuvant is not disclosed or claimed as wetting agent, emulsifying agent, or suspending agent.

Because neither Sham nor Sakagami discloses an adjuvant in the immunological sense as used in the claims, Applicant asserts that their combination cannot render the rejected claims obvious because not all elements of the rejected claims are taught.

Second, Applicant asserts that neither Sham nor Sakagami provides the required motivation to combine the references. The Examiner cites three rationales for combining the pine cone extract of Sakagami with the HIV vaccine of Sham.

With respect to the alleged teaching of Sham that the anti-HIV compound taught by Sham may be "beneficially"

administered in combination with a pine cone extract and/or with a vaccine such as an HIV vaccine (at p.6, ¶ 1 of the Office Action), Applicant notes that pine cone extract is taught (col. 75, line 66) as part of an exhaustive list of materials known in the art as treatments for HIV or for diseases occurring in individuals with HIV/AIDS. Sham does not teach any benefit to administration of these combinations: Sham merely teaches that these materials may be administered together with anti-HIV compounds. In particular, Sham does not provide any motivation to administer pine cone extract as an adjuvant for a vaccine, because immunological adjuvants are not taught, and neither is any benefit of this combination taught or suggested. Thus, Applicants assert that neither Sham nor Sakagami teaches the desirability of the combination and that the Examiner is applying impermissible hindsight or an impermissible "obvious to try" standard in combining the references. MPEP 2144.06 and In re Geiger, 815 F.2d 686, 2 USPQ2d 1276 (Fed. Cir. 1987).

With respect to the Examiner's assertion that the teaching of Sakagami of pine cone extract possessing "beneficial immunopotentiating activity" provides a motivation to combine Sham and Sakagami, Applicant respectfully disagrees. At col. 4, lines 63-65, Sakagami teaches that immunopotentiating activity of pine cone extract is manifested by activation of human peripheral blood monocytes and polymorphonuclear cells. Applicants assert that such activity is unrelated to the immunological adjuvant property of pine cone extract of their

invention, and therefore cannot provide a motivation to combine Sham and Sakagami. Specifically, Applicant notes that activation of human peripheral blood monocytes and polymorphonuclear cells constitutes activation of the innate immune system, which is distinct from the activation of the adaptive immune system, and does not rely upon previous contact with an antigen to mount an immune defense. In contrast, antigen specific recognition with subsequent clonal expansion is required in the adaptive immune system. More specifically, the purpose of vaccines and their adjuvants is to stimulate the adaptive immune system to mount an antigen-specific response: monocytes and polymorphonuclear cells cannot mount such a response. Therefore, the teaching of immunopotentiality by Sakagami does not suggest that pine cone extract would be an adjuvant. Consequently, it cannot provide a motivation to combine the references, nor a reasonable expectation of success in doing so.

With respect to the Examiner's suggestion that it would have been prima facie obvious to combine pine cone extract and a vaccine because each is allegedly taught separately for the same purpose, Applicant respectfully disagrees. The essence of the present invention is that pine cone extract significantly enhances antigenicity of a vaccine resulting in a superior immune response to vaccination: pine cone extract is claimed as an adjuvant and for that purpose. In contrast, the art cited by the Examiner teaches pine cone extract as a therapeutic agent in



its own right and not for the purpose of enhancing the effectiveness of a vaccine. Under the standard of In re Kirkhoven, cited by the Examiner it is prima facie obvious to combine two compositions where each is taught by the prior art to be useful for the same purpose, in order to form a composition to be used for "the very same purpose." Here, the purpose for which pine cone extract is taught in the prior art is not "the very same purpose" for which the combination is now claimed. Accordingly, Applicant asserts that the combination is not prima facie obvious.

Third, Applicant asserts, that there would have been no reasonable expectation of success that pine cone extract would have acted as an adjuvant in a vaccine because, for the reasons given above, pine cone extract is not taught or suggested as having adjuvant properties within the immunological meaning of the term.

Applicants therefore respectfully request that the rejection of Claims 3, 4, 7, 8, and 10-12 under 35 U.S.C. §103(a) be withdrawn.

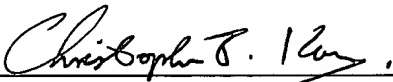
There being no further rejections, favorable consideration and early issuance of the Notice of Allowance are respectfully requested. Should further issues remain that the Examiner believes may be addressed by telephone, the Examiner is respectfully requested to contact the undersigned at the

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